

# THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH EPIGASTRIC PAIN ACCESSING TO AN EMERGENCY DEPARTMENT

A. Saviano<sup>2</sup>, C. Petruzzello<sup>3</sup>, A. Piccioni<sup>1</sup>, M. Brigida<sup>2</sup>, G. Pignataro<sup>1</sup>,  
M. Covino<sup>1</sup>, M. Candelli<sup>1</sup>, M. Fuorlo<sup>1</sup>, A. Migneco<sup>1</sup>, V. Ojetti<sup>1,2</sup>

<sup>1</sup>Emergency Department, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy

<sup>2</sup>Università Cattolica del Sacro Cuore, Rome, Italy

<sup>3</sup>Emergency Department, Ospedale Cristo Re, Rome, Italy

Corresponding Author: Veronica Ojetti, MD, Ph.D; e-mail: veronica.ojetti@unicatt.it

**Abstract – Objectives:** *Helicobacter pylori* (HP) infection is responsible of epigastric pain and dyspepsia. Many people suffering from HP infection experience acute retrosternal pain similar to a heart attack, and they access the Emergency Department (ED). The aim of this study is to evaluate the prevalence of HP infection in patients accessing the ED for epigastric/chest pain and/or dyspepsia in the absence of alarm symptoms, and to demonstrate the efficacy and utility of a rapid 13C-Urea Breath Test (UBT) directly in the ED.

**Patients and Methods:** We enrolled 101 consecutive patients (43M/58F, mean age  $41.8 \pm 15.9$ ) who came to the ED of Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome with epigastric pain and dyspepsia. We excluded patients with chronic use of PPI, and recent use of antibiotics or antacids. Patients, in addition to the normal diagnostic protocol for epigastric pain, performed a UBT for the rapid diagnosis of HP.

**Results:** 36/101 (35.6%) patients resulted positive to HP infection, with a mean delta over the baseline (DOB) of  $28.2 \pm 11.3$ . All other exams were negative for 31/36 (86.0%) HP positive patients. Among the HP negative patients, 6/65 (9.3%) had gallbladder's stones, 3/65 (4.6%) had electrocardiogram (EKG) abnormalities, 2/65 (3.1%) had a pancreatitis, 3/65 (4.6%) had a pneumonia, 5/65 (7.7%) had gastroenteritis, 16/65 (24.6%) musculoskeletal pain and 28/65 (43.1%) had reflux disease. The use of UBT in ED had a positive predictive value of 91.3%, with a sensitivity of 100% and a specificity of 95% in the detection of HP infection in patient with epigastric pain compared to other etiologies of epigastric pain.

**Conclusions:** The use of the UBT in patients accessing the ED for epigastric/chest pain and/or dyspepsia, in absence of alarming symptoms, allows obtaining a rapid, reliable and non-invasive diagnosis of HP infection as a responsible cause for the symptoms. This allows an early diagnosis and the prescription of an eradication therapy at the time of discharge, reducing ED overcrowding and the relative costs.

**Keywords:** Epigastric pain, *Helicobacter pylori*, Dyspepsia, Urea breath test, Emergency Department.

## INTRODUCTION

*Helicobacter pylori* (HP) is a gram-negative bacterium that can colonize the gastric mucosa<sup>1</sup>. It represents one of the most prevalent infections worldwide<sup>2</sup>. According the US Centers for Disease Control, about 2/3 of the world's population is infected with HP. Different tests are available to



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detect *HP* infection and they should be chosen on the base on age, symptoms, home therapy, etc.<sup>3-5</sup>. After detecting *HP* infection, it is essential to eradicate it, since it is associated to several complications as peptic ulcer disease, atrophic gastritis, lymphoma, and gastric cancer<sup>6-8</sup>. Patients suffering from *HP* infection can present dyspepsia, postprandial fullness, burning sensation, early satiety or epigastric pain<sup>4,9,10</sup>. This last is the most common symptom. It arises especially between meals and in the early morning (when the stomach is empty), with a duration that can vary from a few minutes to a few hours. Many people reported also acute retrosternal pain completely similar to an attack of angina pectoris, and, for this reason, they come to the Emergency Department (ED). To better manage chest pain<sup>11</sup> in ED, the Italian Society of Emergency Medicine recommend to perform a 12 lead ECG, a blood dosage of troponin levels, chest X-ray and eventually a cardiac stress test to exclude acute coronary syndrome (ACS)<sup>12</sup>. Epigastric pain represents a challenge for emergency physicians, since it can hide cardiovascular diseases. In Italy, more than 5 million of people/year are admitted to the ED for acute chest pain, accounting for approximately 5-9% of all adult patient visits not related to traumatic reasons<sup>13,14</sup>. Of these patients, the majority do not have ACS and in the most of cases, the EKG is not diagnostic<sup>15</sup>. In the context of emergency, the gastrointestinal causes as explanation of epigastric pain, rank in third position with a percentage of 6%, after the cardiac etiologies of epigastric-chest pain 45% and the musculoskeletal one 14%<sup>11,12,16</sup>. A rapid diagnosis of *HP* infection and its treatment are essential to reduce the overcrowding of ED and to discharge safely patients with prescription of a home eradication therapy<sup>17</sup>. Different tests are available for detecting *HP* infection<sup>18,19</sup>. There is invasive test, such as serological tests and endoscopy, and non-invasive test, such as <sup>13</sup>C-urea breath test (UBT) and fecal antigen of *HP* (HPS AG) with both a high sensitivity and specificity around 94-98%. Endoscopy with biopsies is considered the optimal standard for ulcer diagnosis, gastric cancer diagnosis or gastrointestinal bleeding, but its costs do not justify its use in all patients accessing the ED with dyspepsia<sup>7,9,17</sup>. So, UBT and HPS AG remains the fastest, easiest and less expensive test to use in the ED to detect the *HP* infection<sup>20</sup>. The possibility of collect stool during a visit in ED and to analyze in a laboratory open 24 hour is not easy in the clinical practice. However, it is easier to collect breath and analyze it directly in the ED with a small infrared photometry. In case of positivity an antibiotic treatment plus a proton pump inhibitors (PPI) could be prescribed directly in ED. Treatment lasts for 1-2 week. If it is carried out regularly, the therapy is effective in 90% of cases<sup>21,22</sup>. The aim of our study was to evaluate the presence of *HP* infection in patients admitted to the ED for epigastric pain and dyspepsia in the absence of alarm symptoms. Our study showed the efficacy and usefulness of the rapid UBT tool for an easy diagnosis of *HP* infection in patients who access the ED reporting dyspepsia. Moreover, this study provided a rapid etiological diagnosis of patients with epigastric pain in the emergency room. Therefore, the emergency physicians can be confident to discharge patients with an eradication therapy of *HP*, reducing the hospitalization-costs and the overcrowding of the ED.

## PATIENTS AND METHODS

From September 2019 to September 2020, we performed a prospective observational single-center study. We enrolled 101 consecutive patients (43M/58F mean age  $41.8 \pm 15.9$ ) who came to the ED of Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome with epigastric/chest pain within the previous 12 h. They underwent the regular diagnostic protocol for ACS<sup>12</sup> and were subsequently asked to perform the UBT.

### Study Population

We included patients (M/F) aged >18 years or <50 years, fasted for at least 4 hours, with abstinence from smoking for at least 4 hours, who signed the consent to participate to the study.

We excluded patients aged <18 years or >50 years, with alarm symptoms (anemia, weight loss), with acute myocardial infarction, atrial fibrillation at the EKG, who were taking antibiotics within the past 30 days, or PPI continuously for the past 15 days, or antacids within the last 6 hours, and with a known or suspected pregnancy.

Baseline characteristics of patients are showed in Table I.

**TABLE 1. BASELINE CHARACTERISTICS OF PATIENTS PERFORMING UBT IN ED.**

58/101 enrolled patients had no history of diseases.

43/101 enrolled patients had a history of:

- Diabetes → 4 patients
- Hypertension → 11 patients
- Chronic obstructive pulmonary disease → 3 patients
- Coronary artery disease → 5 patients
- Cancer → 4 patients
- Liver diseases → 5 patients
- Use of NSAIDs and aspirin → 8 patients
- Use of NOACs → 3 patients

The patient enrolled in our study performed laboratory diagnostic tests (blood count, biochemistry, coagulation, cardiac markers), EKG and, in addition, the UBT. Patient's data (demographic, home therapy, UBT-DOB value, endoscopy results, biopsies, blood tests, EKG, etc.) were collected in an Excel Database and analyzed using parametric and non-parametric statistical tests. Values of  $p < 0.05$  were considered as significant.

### 13C-Urea Breath Test (UBT)

To perform the UBT we used a commercial brand UBT-Kit (Richen Europe, Milan, Italy). This consists in taking orally one dose of citric acid as a pre-administered test meal and one dose of 75 mg  $^{13}\text{C}$ -labeled urea dissolved in 200 ml of water. Patients drank the content immediately after taking the first breath of exhaled air in a sachet (T0). After 30 minutes, the second breath was collected in another sachet (T30). The patient performed the examination fasting, resting, without drinking, without eating and without smoking. Breath tests were collected in twice, with a concordance of 98.5% (Cohen's test). The exhaled air is then analyzed, within 24 hours, by an infrared spectrometer "IR-force 200" by Beijing Richen-force Science and Technology Co. Ltd., which allows to measure the amount of  $\text{CO}_2$   $^{13}\text{C}$  with respect to the total of expired  $\text{CO}_2$   $^{12}\text{C}$  in three minutes. IR Force – 200 is an instrument designed to guarantee an efficient and rapid response in the diagnosis of *HP* infections with an optimal performance for small and medium routines. The instrument is user-friendly and does not require specialized personnel for its use. The difference in the ratios between the baseline value and the post-urea value is referred to as delta over baseline (DOB). The delta over baseline (DOB)  $> 3.5$  was considered indicative of *HP* infection.

### Ethics Statement

The study was conducted in accordance with the European Union Standards of Good Clinical Practice and the current revision of the Declaration of Helsinki. None of the patients or authors received any honorary or economic benefits for the participation in this work. The study was approved on 29<sup>th</sup> March 2019 by the Ethical Committee of the Università Cattolica del Sacro Cuore of Rome, with ID 2302, Protocol No. 14245/19.

### Statistical Analysis

A descriptive statistical analysis was performed using absolute and relative frequencies, mean and standard deviation (SD), when appropriate, for demographic and clinical characteristics of surveyed patients and clinical outcome parameter. The statistical significance level was set at  $p < 0.05$  and all the analyses were carried out by using the software "Stata MP 14 for Mac" (Stata Corp., Lakeway, TX, USA).

## RESULTS

We found that 36/101 (35.6%) patients resulted positive to *HP* infection while 65/101 (64.4%) resulted negative. The mean DOB value was of  $28.2 \pm 11.3$  with a significant difference between males and females. The mean DOB value for males was  $26.7 \pm 10.2$  compared to  $30.1 \pm 15.8$  in females.

In 31/36 *HP* positive patients (86.0%) all other exams were negative, meanwhile in the other 6/36 *HP* positive patients (13.4%) were found also stones in the gallbladder and 2/36 (0.6%) positive patients performed gastroscopy with the detection of a bleeding peptic ulcer.

As regards *HP* negative patients, 6/65 (9.2%) had gallbladder's stones, 3/65 (4.6%) had EKG abnormalities, 2/65 (3.1%) had a pancreatitis, 3/65 (4.6%) had pneumonia, 5/65 (7.7%) had gastroenteritis, 2/65 (3.1%) had pneumothorax, 16/65 (24.6%) had musculoskeletal pain and 28/65 (43.1%) had reflux disease.

15/101 (14.8%) patients performed a gastroscopy with detection of esophagitis (in 4 patients), erosive gastritis (in 6 patients), peptic ulcer (in 5 patients).

29/101 (29.7%) patients were hospitalized, while 71/101 (70.3%) were safely discharged from ED (Figure 1).

Among hospitalized patients, 8 resulted positive to UBT (6 *HP* positive patients were hospitalized for gallbladder stones and 2 *HP* positive patients for bleeding ulcer). The remaining 22 hospitalized patients resulted negative to UBT test and were hospitalized for other reasons (6 for gallbladder stones, 3 for EKG abnormalities, 2 for acute pancreatitis, 3 for pneumonia, 5 for gastroenteritis, 2 for pneumothorax and 1 for musculoskeletal disease).

We found that nobody of the discharged patients was back to the ED for the same symptoms or pathology within the next 30 days.

The use of UBT in ED had a positive predictive value of 91.3%, with a sensitivity of 100% and a specificity of 95% (Table 2). The test gave a result (positive or negative) in all the patients examined.

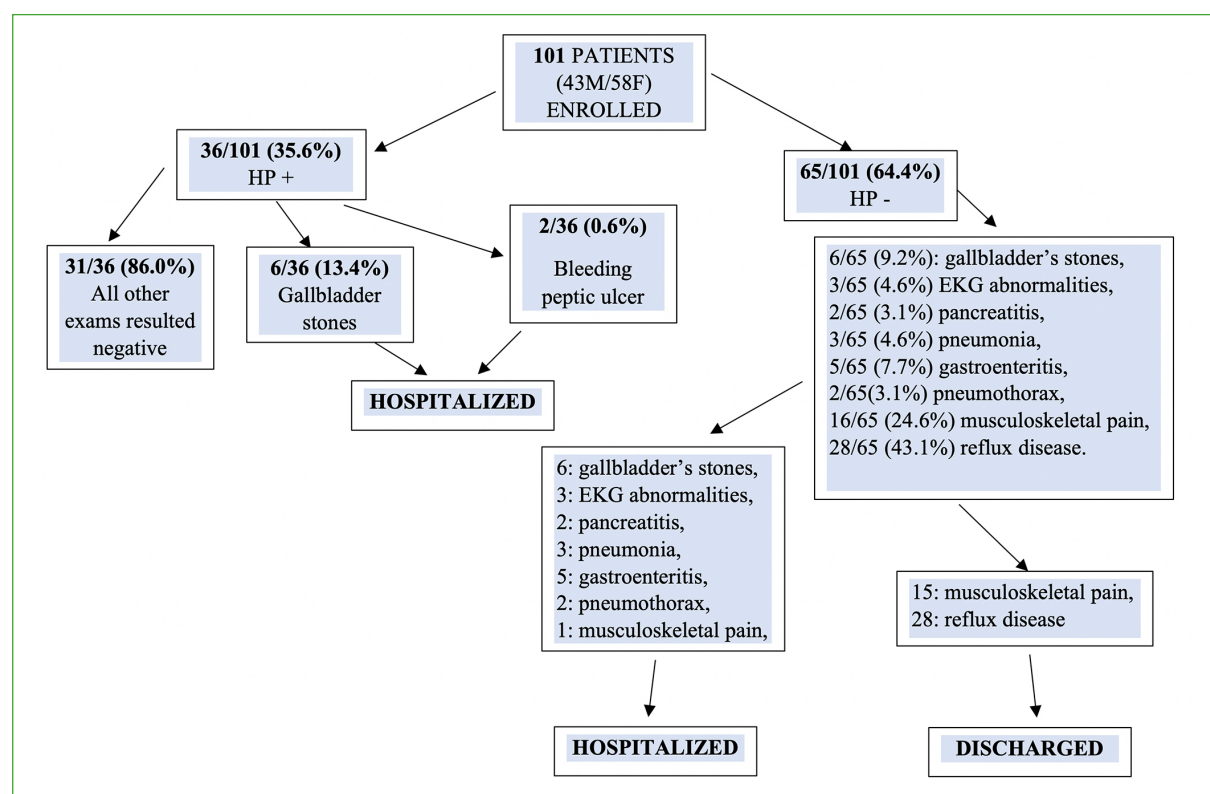


Figure 1. Patients' stratification according to UBT results.

TABLE 2. VALIDITY PARAMETERS OF UBT FOR THE DIAGNOSIS OF *HP* INFECTION IN ED.

Positive Predictive Value	91.3%
Sensitivity	100%
Specificity	95%
Cut-Off (DOB)	3.5

## DISCUSSION

Our study shows that approximately 1/3 of ED patients with epigastric/chest pain had *HP* infection with a significant higher DOB value in females compare to males. This is well documented in other studies, maybe linked to some hormonal differences<sup>2</sup>. Previous studies performed in outpatients setting showed that the *test and treat strategy* decrease morbidity and promote cost-effective care<sup>20</sup> in higher prevalence country. In Italy, we have a high prevalence of *HP* infection, so the strategy could be applied also in ED, with a benefit both for patients and for health care systems. We showed that UBT is a simple test to utilize in the ED because of the tolerability, easiness to perform and for rapid results. In ED setting, UBT is better than serum antibodies test, stool antigen test or upper endoscopy. The determination of serum antibodies is not able to distinguish between an active or non-active infection. As regards stool test, it is not easy to obtain a sample during ED visit. Upper gastrointestinal (GI) endoscopy has to be reserved to patient with upper GI bleeding. The most important benefit linked to the test and treat strategies for patients with epigastric/chest pain in the ED could be, as we demonstrate, eradication treatment prescribed immediately after the visit in the ED because those patients had no other diseases associated. On the contrary, patients who tested negative for *HP* infection had other pathologies as gallbladder's stones, EKG abnormalities, pancreatitis, pneumonia, gastroenteritis, reflux disease, etc. So, carrying out the UBT (directly in the ED) is therefore essential to reduce the prolonged treatment with PPI, the incidence of *HP* related-complications (such as gastric cancer and peptic ulcers) and to decrease the cost of invasive procedures, such as upper endoscopy and, at the end, to discharge the patient safely without worrying about having overlooked other diagnosis. On the other hand, a negative UBT test, must prompt the emergency physician to look for other causes to explain the patient's symptoms. With this background and considering its simplicity, quickness, cost-effectiveness and qualitative validity, we consider UBT an optimal diagnostic test to be applied directly in the ED. The main limitation of our study is that it is monocentric and other ED may have a different rate of *HP* infection depending on the different populations.

## CONCLUSIONS

The use of the UBT in patients accessing the ED for epigastric pain and dyspepsia, in absence of alarming symptoms, allows obtaining a rapid, reliable and non-invasive diagnosis of *HP* infection as a responsible cause for the symptoms. This allows an early diagnosis and the possibility to prescribe an eradication therapy at the time of discharge, reducing the ED overcrowding and the relative costs.

### Author Contributions

Conceptualization: V Ojetti; methodology and writing: A Saviano; software: G Pignataro, A Piccioni, M Covino, C Petruzzello; validation and formal analysis: M Covino, C Petruzzello; investigation: G Pignataro M Fuorlo, A Saviano; resources: A Migneco; data curation: V Ojetti, A Migneco, M Brigida, A Saviano; revision: M Brigida, A Saviano; editing: V Ojetti, M Candelli; visualization: V Ojetti; supervision: V Ojetti.

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### Conflict of Interest

All authors declare no conflict of interest.



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